AWARD NUMBER: W81XWH-14-2-0170

TITLE: A Randomized, Crossover Clinical Trial of Exoskeletal-Assisted Walking to Improve Mobility, Bowel Function, and Cardiometabolic Profiles in Persons with SCI

PRINCIPAL INVESTIGATOR: Ann M. Spungen, EdD

CONTRACTING ORGANIZATION: Bronx Veterans Medical Research Foundation
Bronx, NY 10468

REPORT DATE: October 2017

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command

Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
October 2017	Annual	29Sep2016-28Sep2017

4. TITLE AND SUBTITLE
Randomized, Crossover Clinical Trial of Exoskeletal-Assisted Walking to Improve Mobility, Bowel Function, and Cardiometabolic Profiles in Persons with SCI

5a. CONTRACT NUMBER
W81XWH-14-2-0170

5b. GRANT NUMBER
SC130234

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Ann M. Spungen, EdD (Principal Investigator)
E-Mail: ann.spungen@va.gov

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

BRONX VETERANS MEDICAL
RESEARCH FOUNDATION
130 W KINGSBRIDGE RD
STE 1F01
BRONX NY 10468-3904

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

The primary objective is to achieve specific walking velocities and distances using a powered exoskeletal over the course of 12 and 36 sessions in 3 months in people with chronic SCI who are wheelchair users for community mobility. The secondary objectives are to determine if this amount of exoskeletal-assisted walking is effective in improving bowel function and body composition. Exploratory objectives include questions concerning the retention or non-retention of the positive changes, effects of increased physical activity on vagal tone, orthostatic tolerance, lipid profile, total testosterone, estradiol levels, and quality of life. To date (Y3 of the study), the enrollment breakdown is: 78 participants consented for Screening: 55 participants were randomized and 22 were screen failures. The Screening failure reasons include: 12 for low bone mineral density, 4 contractures, 1 severe spasticity, 4 schedule conflicts or unable to participate, and 1 other. Twenty-seven participants have completed the study, 11 have withdrawn, 11 are currently enrolled, and 9 more are in the pre-screening process. Preliminary data has been analyzed for 27 participants for the walking tests at sessions 12 and 36. Twenty-two participants have been analyzed for lipid profile, body composition, and bowel and bladder outcomes.

15. SUBJECT TERMS
Exoskeletal Assisted Walking (EAW), Mobility, Bowel Function, Cardiometabolic profile

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
Unclassified	Unclassified	Unclassified	Unclassified	22	19b. TELEPHONE NUMBER *(include area code)*

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

Table of Contents

Page

1. INTRODUCTION:

The primary objectives of this proposal are to achieve successful walking skills in the exoskeletal-assisted walking devices for an extended period of time and at specific velocities and distances over the course of 36 sessions in three months in people with chronic SCI who are wheelchair users for community mobility. The secondary objectives are to determine if 36 sessions in three months of walking is effective in improving bowel function and body composition. The exploratory objectives are to address additional questions concerning the retention or non-retention of positive changes, the effects of the increased physical activity from exoskeletal-assisted walking on vagal tone, orthostatic tolerance, lipid profile, total testosterone, estradiol levels, and quality of life (QOL).

2. KEYWORDS:

Powered exoskeletons, paraplegia, tetraplegia, high density lipoprotein, lipid profile, orthostatic tolerance, total testosterone, estradiol, quality of life, ReWalk, and Ekso

3. ACCOMPLISHMENTS:

What were the major goals of the project?

On September 30, 2017 month 36 of the study was completed. The goals for these 36 months are as follows:

Major Task 2: Study recruitment and enrollment.

Subtask 4: Randomize the next 8/6/4 participants at each respective Site (Randomize a total of 48 between study months 25 to 33).

Response: We have randomized 45 of 48 participants (94%) by month 33 of the study.

Subtask 5: Randomize the next 8/6/4 participants at each respective Site (Randomize a total of 64 participants between study months 34 to 42).

Response: We have randomized 55 of 64 (86%) with Y4 Q2 still ahead of us. We have about 15 participants in pre-screening, of which we anticipate randomizing 9 by March 30, 2018. These last 9 participants to be enrolled will bring us to 100% of our enrollment goals (55 + 9 = 64). We recognize that to achieve 100% enrollment we are 6 months behind the projected dates, but we believe these last nine participants can be completed during Q3, Year 4 (by 6/30/2018) of the study.

Major Task 3: Review/complete data forms, data edits and entry

Response: We have completed 75% of the review of the data entry for missing values and errors. This is an ongoing process. We have completed 100% of the data entry for 27 participants to date and about 50% of all data entry for the 55 participants that have been randomized to date

Major Task 4: Review and analyze data

Subtask 2: Analyze preliminary data for primary outcomes (months 24 to 38)

The Primary Aims consist of the following:

1. By session 12 (first month of WALK training), the participants will be able to perform the following exoskeletal-assisted walking tests with or without minimal assistance:

Response: In 27 participants who have been completed to date the following percentages for each aims were achieved.

a. 10m WT
    i. 90% in ≤60 seconds (≥0.17 m/s);
    Response: 89% (24 of 27) have achieved this goal.
    ii. 10% in ≤40 seconds (≥0.25 m/s);
    Response: 56% (15 of 27) have achieved this goal.
b. 6min WT
    i. 80% at a distance ≥50 m (≥0.14 m/s);
    Response: 93% (25 of 27) have achieved this goal.
    ii. 20% at a distance ≥80 m (≥0.22 m/s);
    Response: 63% (17 of 27) have achieved this goal.
c. TUG
    i. 80% in ≤120 seconds);
    Response: 93% (25 of 27) have achieved this goal.
    ii. 20% in ≤90 seconds);
    Response: 67% (18 of 27) have achieved this goal.

2. By session 36 (three months of WALK training), participants will have improved their ability to walk faster and longer distances and will be able to perform exoskeletal-assisted walking tests with or without minimal assistance as follows:
    a. 10m WT - 70% in ≤40 seconds (≥0.25 m/s);
    Response: 74% (20 of 27) have achieved this goal.
    b. 6min WT - 70% at a distance ≥80 m (≥0.22 m/s);
    Response: 78% (21 of 27) have achieved this goal.
    c. TUG - 60% in ≤90 seconds;
    Response: 85% (23 of 27) have achieved this goal.

Subtask 3: Submit abstracts with preliminary data for primary outcomes for national meetings (months 24 to 38).
Response: Dr. Spungen presented this data at the International Spinal Cord Society (ISCOS) 2017 annual meeting in Dublin, Ireland on October 26, 2017.

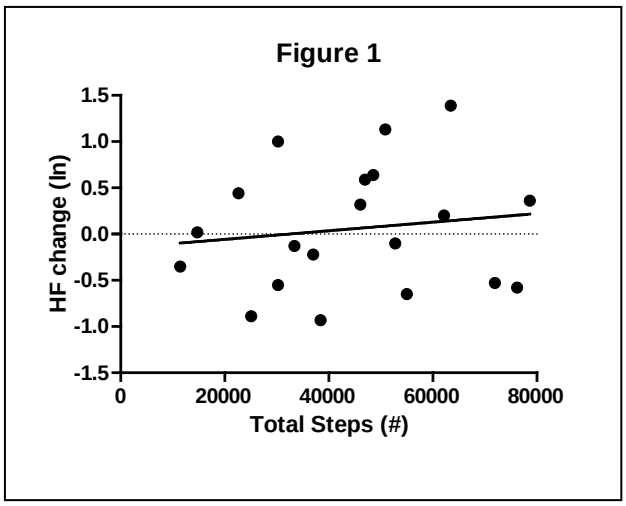
Subtask 4: Analyze preliminary data for secondary outcomes (months 24 to 40)
The Secondary Aims are to affect the following by three months of exoskeletal-assisted walking (WALK):

1. To improve bowel function as measured by established survey instruments; and
2. To reduce total body fat mass and percent as measured by DXA.

Response: Bowel function was reported in 22 participants at the ISCOS 2017 annual meeting. Fat and lean masses were reported in 22 participants at the ISCOS 2017 annual meeting. Please see attached slide presentation for data on both variables (Appendix 1).

Subtask 5: Analyze preliminary data for exploratory outcomes (months 24 to 40)

Response: We have analyzed some preliminary data on vagal tone on 22 participants. With exercise training we anticipate improvements in cardiac vagal tone, which can be estimated non-invasively using the high frequency (HFln) component of heart rate variability (HRV). Data collection has been completed in 20 subjects at pre- mid- and post-EAW training. We examined the relationship between change (from pre- to post-EAW training) in HFln and the total number of steps taken over the course of the EAW training (**Figure 1**) and the average number of steps taken per training session (**Figure 2**). These preliminary data do not support an advantageous role of EAW training on cardiac vagal tone in the small cohort of subjects with SCI who have completed testing. Data collection is ongoing and we anticipate increases in 24-hour HFln following EAW training in persons with SCI which may be dependent on the total number of steps and compliance to the study protocol.



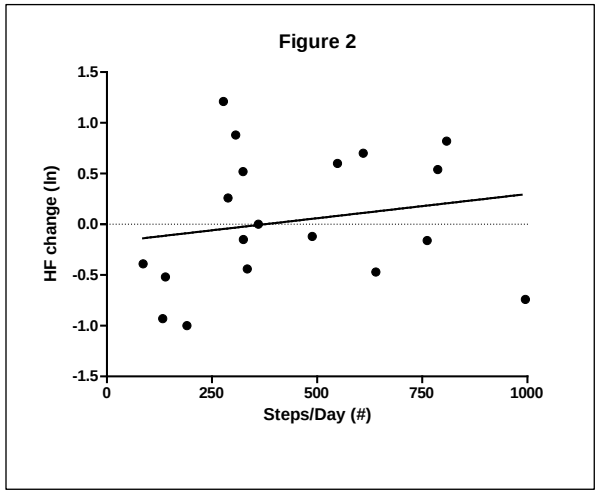


Figure 1 displays the relationship between the number of steps taken over the course of the EAW training and the change in the 24-hour high frequency (HFln) component of heart rate variability (HRV) [r^2=0.01846; p=ns]. **Figure 2** displays the relationship between the number of steps taken per study visit (steps/day) and the change in the 24-hour HFln component of HRV [r^2=0.03656; p=ns].

Response: High density lipoprotein cholesterol (HDL-c) was analyzed in 21 participants. Please see the ISCOS 2017 slide presentation for the HDL-c results (Appendix 1).

What was accomplished under these goals? Please see written "responses" above after each goal and the following Statement of Work (Table 1), Projected and Actual Enrollment (Table 2) and Detailed Screening, Randomization, and Reasons for Screen Failures and Withdrawals (Table 3).

Table 1. Statement of Work	Timeline (months)	Percent Completed	Date Completed
Major Task 1: Study start-up and continuation administrative functions			
Subtask 1: Prepare Regulatory Documents and Research Protocol	1 to 3	100%	30-Dec-14
If Applicable, coordinate with Sites for CRADA* submission	n/a	n/a	n/a
If Applicable, coordinate with Sites for material transfer agreements (MTAs) or clinical trial agreements (CTAs) submission	n/a	n/a	n/a
If Applicable, coordinate with Sites for nondisclosure agreements (NDAs).	n/a	n/a	n/a
If applicable, indicate time required for submission and exemption of an Investigational Device Exemption (IDE) application to the U.S. Food and Drug Administration	1 to 3	100%	30-Dec-14
Refine eligibility criteria, exclusion criteria, screening protocol	1 to 3	100%	30-Dec-14
Finalize consent form & human subjects protocol	1 to 3	100%	30-Dec-14
Coordinate with Sites for Local IRBs** protocol submission	1 to 3	100%	30-Dec-14
Coordinate with Sites for University IRB** review	1 to 6	100%	30-Dec-14
Coordinate with Sites for Military 2nd level IRB** review (ORP/HRPO)	1 to 6	100%	30-Dec-14
Submit amendments, adverse events and protocol deviations as needed	As needed	ongoing	ongoing
Coordinate with Sites for annual IRB** report for continuing review	Annually	ongoing	ongoing
*Milestone Achieved: Local IRB** approval at BVMRF, UMROI, and KFRC*	3	100%	30-Mar-15
*Milestone Achieved: HRPO*** approval for all protocols and local IRB** approvals.*	6	100%	30-Mar-15
Subtask 2: Coordinate with Sites for job descriptions design	1 to 3	100%	30-Dec-14
Advertise and interview for project related staff	1 to 3	100%	30-Dec-14
Coordinate for space allocation for new staff	1 to 3	100%	30-Dec-14
Coordinate with Sites for hiring and training of staff	1 to 6	100%	30-Dec-14
Coordinate with Sites for providing standard training procedures among exoskeletal-trainers	1 to 6	100%	30-Dec-14
Milestone Achieved: Research staff hired and begin staff training	6	100%	30-Dec-14
Subtask 3: Facilitate and Coordinate with Sites for hiring, training, supervision and fidelity checks as needed for study participant attrition	6 to 48	100%	30-Dec-14
Coordinate multi-site training meeting for exoskeletal training, walking assessments standardization, data collection paper forms, data collection web-based forms, and use of log record	3 to 6	100%	9-Apr-15

Table 1. Statement of Work	Timeline (months)	Percent Completed	Date Completed
PI, Lead Engineer and Study Coordinator travel to Sites for staff training of procedures	3 to 6	100%	9-Apr-15
Coordinate multi-site training meeting for standardization of SCI QOL and bowel function assessments	3 to 6	100%	9-Apr-15
Coordinate multi-site training meeting for blood draw procedures (fasting condition, amounts, tubes, mailing to Quest Diagnostics)	3 to 6	100%	9-Apr-15
Coordinate multi-site training meeting for orthostatic tolerance test and Holter monitor assessment	3 to 6	100%	9-Apr-15
Coordinate with Sites for training to maintain 100% concordance with Study protocol	6 to 48	100%	9-Apr-15
Milestone Achieved: Maintained trained Study staff throughout duration of the clinical trial	6 to 48	100%	9-Apr-15
Major Task 2: Study recruitment and enrollment			
Subtask 1: Begin participant screening and consenting process	6 to 7	100%	11-May-15
Milestone Achieved: Participant #1 consented, randomized and enrolled at each Site	6 to 7	100%	14-Aug-15
Subtask 2: Randomize the first 4 participants at each respective Site	7 to 15	100%	22-Sep-15
Complete participant baseline evaluations	7 to15	100%	10-Oct-15
Complete participant weekly and monthly evaluations	7 to 15	100%	1-Apr-16
Complete participant post evaluations	7 to 15	100%	1-Apr-16
Milestone Achieved: 12 participants consented, screened, randomized, and enrolled for the study	7 to 15	100%	22-Sep-15
Subtask 3: Randomize the next 8/6/4 participants at each respective Site	16 to 24	100%	1-Oct-16
Complete participant baseline evaluations	16 to 24	100%	1-Oct-16
Complete participant weekly and monthly evaluations	16 to 24	100%	1-Mar-17
Complete participant post evaluations	16 to24	100%	1-Mar-17
Milestone Achieved: 30 participants consented, screened, randomized, and enrolled for the study	16 to 24	100%	1-Mar-17
Subtask 4: Randomize the next 8/6/4 participants at each respective Site	25 to 33	100%	1-Dec-17
Complete participant baseline evaluations	25 to 33	100%	1-Dec-17
Complete participant weekly and monthly evaluations	25 to 33	79%	ongoing
Complete participant post evaluations	25 to 33	79%	ongoing
Milestone Achieved: 48 participants consented, screened, randomized, and enrolled for the study	25 to 33	79%	ongoing
Subtask 5: Randomize the next 8/4/4 participants at each respective Site	34 to 42	86%	ongoing
Complete participant baseline evaluations	34 to 42	86%	ongoing
Complete participant weekly and monthly evaluations	34 to 42	86%	ongoing
Complete participant Post 1 evaluations	34 to 42	75%	ongoing
Complete participant Post 2 evaluations	34 to 42	50%	ongoing

Table 1. Statement of Work	Timeline (months)	Percent Completed	Date Completed
Milestone Achieved: 64 participants consented, screened, randomized, and enrolled for the study	34 to 42	86%	ongoing
Subtask 6: Complete training and testing of any remaining participants at each respective Site	43 to 45	50%	ongoing
Complete participant weekly and monthly evaluations	43 to 45	50%	ongoing
Complete participant post evaluations	43 to 45	50%	ongoing
Milestone Achieved: All participants at each respective Site completed	43 to 45	50%	ongoing
Major Task 3: Review/complete data forms, data edits and entry			
Subtask 1: Ongoing review of data entry	7 to 45	75%	ongoing
Subtask 2: Ongoing review of adverse and serious adverse	6 to 45	75%	ongoing
Subtask 3: Ongoing data edits for missing values	7 to 45	75%	ongoing
Subtask 4: Ongoing review for data entry errors	7 to 45	75%	ongoing
Subtask 5: Complete all data entry	43 to 45	50%	ongoing
Milestone Achieved: Data entry is completed in the data base	45	50%	ongoing
Major Task 4: Review and analyze data			
Subtask 1: Review of data / analyze data	7 to 15	100%	1-Oct-15
Review data for problems	7 to 15	100%	1-Oct-15
Make necessary protocol adjustments (if needed)	7 to 15	100%	1-Oct-15
Perform sub analyses of walking tests and activity logs in first 12 participants	15 to 16	100%	1-Dec-15
Milestone Achieved: Data reviewed for necessary adjustment	7 to 15	100%	1-Oct-15
Subtask 2: Analyze preliminary data for primary outcomes	24 to 38	75%	ongoing
Perform sub analyses of walking tests and activity logs in the first 20 to 38 participants	24 to 38	75%	ongoing
Subtask 3: Submit abstracts with preliminary data for primary outcomes for national meetings	24 to 38	75%	ongoing
Milestone Achieved: Abstract presentations of preliminary data	28 to 38	75%	ongoing
Subtask 4: Analyze preliminary data for secondary outcomes	24 to 40	75%	ongoing
Perform sub-analyses of body fat mass in the first 30 to 48 participants	24 to 36	75%	ongoing
Subtask 5: Analyze preliminary data for exploratory outcomes	24 to 40	50%	ongoing
In Group 1, perform sub analyses of body fat mass at 3 months follow-up in first 15 to 24 participants	24 to 40	50%	ongoing
Perform sub analyses of blood pressure tests and Holter monitor in the first 30 to 48 participants	25 to 36	50%	ongoing
Perform sub analysis of lipids, and endocrine outcome variables in the first 30 to 48 participants	25 to 36	50%	ongoing

Table 1. Statement of Work	Timeline (months)	Percent Completed	Date Completed
Perform sub analyses of SCI-QOL and bowel function assessments in first 30 to 48 participants	25 to 36	50%	ongoing
Major Task 5: Prepare and write manuscripts			
Subtask 1: Prepare and write manuscripts on full data set of participants	43 to 48		
Prepare and write manuscript of the primary outcomes	43 to 48		
Prepare and write manuscript of the secondary outcomes	43 to 48		
Prepare and write manuscripts for the exploratory outcomes	43 to 48		

Table 2. Projected and Actual Enrollment

Year:	Year 1				Year 2				Year 3				Year 4			
Dates:	(Oct 1, 2014 to Sep 30 2015)				(Oct 1, 2015 to Sep 30 2016)				(Oct 1, 2016 to Sep 30 2017)				(Oct 1, 2017 to Sep 30 2018)			
Quarter:	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Cum. Month:	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48
Quarter Months:	(10/1-12/30)	(1/1-3/30)	(4/1-6/30)	(7/1-9/30	(10/1-12/30)	(1/1-3/30)	(4/1-6/30)	(7/1-9/30	(10/1-12/30)	(1/1-3/30)	(4/1-6/30)	(7/1-9/30	(10/1-12/30)	(1/1-3/30)	(4/1-6/30)	(7/1-9/30)
			Projected		Actual	Projected		Actual	Projected		Actual	Projected	Actual	To be enrolled	Carry-over	
BVMRF			4		3	8		8	8		8	8	6	3		
UMROI			4		2	6		7	6		6	4	2	4		
KF			4		3	4		4	4		4	4	2	2		
Sub Totals			12		8	18		19	18		18	16	10	9		
Cumulative Totals			12		8	30		27	48		45	64	55	64		

Table 3.
Detailed Screening, Randomization and Reasons for Screen Failures and Withdrawls

	BRONX	UMROI	Kessler	Total	
Number Pre-screened	45	21	38	**104**	
Number Consented for Screening	45	21	12	**78**	
Number Screen failed	18	4	0	**22**	28.2%
Number Randomized	26	17	12	**55**	70.5%
Number Completed	14	5	8	**27**	
Number Withdrew	2	6	3	**11**	
Number Currently Enrolled	8	2	1	**11**	
Number in Pre-Screening	3	2	4	**9**	
Reasons for Screen Failures					
Low BMD/FxHx	8	4	0	**12**	15.4%
Contractures	4	0	0	**4**	5.1%
Severe spasticity	1	0	0	**1**	1.3%
Schedule conflict/unable	4	0	0	**4**	5.1%
Other	1	0	0	**1**	1.3%
Reasons for Withdrawals					
Schedule conflict/unable	0	3	2	**5**	
Medical (study related)	0	1	0	**0**	
Medical (non-study related)	2	2	1	**5**	

Note: Of the total group screened, 28.2% were Screen Failures and 70.5% were randomized. Of the 78 Screened, 15.4% failed on the bone criteria, 5.5% failed on contractures and 5.1% failed on schedule conflicts or unable to continue.

What opportunities for training and professional development has the project provided?

This project was not intended to provide a training opportunity. However the PI, Dr. Spungen has used this opportunity to provide professional development for two of her staff: 1) Mr. Steve Knezevic (Doctoral candidate, Rutgers University and Research coordinator for this study) and 2) Dr. Eun-Kyoung Hong (Post-doctoral fellow in Dr. Spungen's lab and the database manager for this study). Dr. Spungen has worked one-on-one with both individuals for analyzing, interpreting, writing, and presenting the data at the Academy of Spinal Cord Injury Professionals (ASCIP) 2017 annual meeting in Denver, CO.

How were the results disseminated to communities of interest?

Response: We have presented at three scientific annual conferences:

1. ASCIP 2017 Platform Presentation, Title: Patient-reported bladder management improvements after exoskeletal-assisted walking. Presenter: EunKyoung Hong, PhD.

2. ASCIP 2017 Poster Presentation, Title: Increased serum high density lipoprotein after 36 exoskeletal-assisted walking sessions. Presenter: Steven Knezevic, MS.

3. ISCOS 2017 Workshop Presentation, Title: Exoskeletal-Assisted Walking in Acute Inpatient and Chronic Outpatient Spinal Cord Injury Rehabilitation. Presenter: Ann M. Spungen, EdD

What do you plan to do during the next reporting period to accomplish the goals?

Response:

Continue with enrollment of the remaining 9 participants.

Complete database entry, edits, and analyses

Prepare manuscripts

4. IMPACT:

Nothing to Report

What was the impact on the development of the principal discipline(s) of the project? Nothing to Report

What was the impact on other disciplines? Nothing to Report

What was the impact on technology transfer? Nothing to Report

What was the impact on society beyond science and technology? Nothing to Report

5. CHANGES/PROBLEMS:

Nothing to Report

Changes in approach and reasons for change Nothing to Report

Actual or anticipated problems or delays and actions or plans to resolve them Nothing to Report

Changes that had a significant impact on expenditures Nothing to Report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents Nothing to Report

Significant changes in use or care of human subjects Nothing to Report

Significant changes in use or care of vertebrate animals Nothing to Report

Significant changes in use of biohazards and/or select agents Nothing to Report

6. PRODUCTS:

Publications, conference papers, and presentations

Response:

1. ASCIP 2017 Platform Presentation, Title: Patient-reported bladder management improvements after exoskeletal-assisted walking. Presenter: EunKyoung Hong, PhD.

2. ASCIP 2017 Poster Presentation, Title: Increased serum high density lipoprotein after 36 exoskeletal-assisted walking sessions. Presenter: Steven Knezevic, MS.

3. ISCOS 2017 Workshop Presentation, Title: Exoskeletal-Assisted Walking in Acute Inpatient and Chronic Outpatient Spinal Cord Injury Rehabilitation. Presenter: Ann M. Spungen, EdD

Journal publications. Nothing to Report

Books or other non-periodical, one-time publications. Nothing to Report

Other publications, conference papers, and presentations. Nothing to Report

Website(s) or other Internet site(s). Nothing to Report

Technologies or techniques. Nothing to Report

Inventions, patent applications, and/or licenses. Nothing to Report

Other Products. Nothing to Report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

Individuals that have worked on the project

Bronx Veterans Medical Research Foundation (BVMRF)		Status
Name:	**Ann M. Spungen, EdD**	No change
Project Role:	Principal Investigator	
Nearest person month worked	1.2	
Contribution to the Project	Principal Investigator	
Funding Support	JJPVAMC	
Name:	**Pierre K. Asselin, MS**	No change
Project Role:	Co-Investigator	
Nearest person month worked	1.2	
Contribution to the Project	Biomedical Engineer	
Funding Support	VA RR&D Center	
Name:	**Stephen D. Kornfeld, DO**	No change
Project Role:	Co-Investigator	
Nearest person month worked	0.6	
Contribution to the Project	Study physician/ medical examinations	
Funding Support	JJPVAMC SCI Service	
Name:	**Jill M. Wecht, EdD**	No change
Project Role:	Co-Investigator	
Nearest person month worked	0.36	
Contribution to the Project	Autonomic and orthostatic outcomes	
Funding Support	JJPVAMC	
Name:	**William A. Bauman, MD**	No change
Project Role:	Co-Investigator	
Nearest person month worked	0.36	
Contribution to the Project	Endocrine outcomes	
Funding Support	JJPVAMC	
Name:	**Steven Knezevic, MS**	No change
Project Role:	Lead Research Coordinator	
Nearest person month worked	6	
Contribution to the Project	Study Coordinator, site primary trainer	
Funding Support	BVMRF and VA RR&D Center	
Name:	**Eun-Kyoung Hong, PhD**	No change
Project Role:	Study Database Manager	
Nearest person month worked	9	
Contribution to the Project	Database developer/manager, Primary trainer	
Funding Support	BVMRF	
Name:	**Denis Doyle-Green**	No change
Project Role:	Research assistant	
Nearest person month worked	6	
Contribution to the Project	Assistant trainer and phlebotomist for study	
Funding Support	BVMRF	
University of Maryland Rehabilitation Orthopedic Institute (UMROI)		**Status**
Name:	**Peter H. Gorman, MD, PhD**	No change
Project Role:	Co-Principal Investigator	
Nearest person month worked	0.6	
Contribution to the Project	Site PI and study physician	
Funding Support	UMROI	
Name:	**Paula R. Geigle, PhD, PT**	No change

Project Role:	Co-Investigator	
Nearest person month worked	0.6	
Contribution to the Project	Physical therapist	
Funding Support	UMROI	
Name:	**William Scott, MA**	No change
Project Role:	Research coordinator	
Nearest person month worked	3	
Contribution to the Project	Primary trainer	
Funding Support	UMROI	
Name:	**Rebecca Webb, PT**	No change
Project Role:	Site research coordinator	
Nearest person month worked	3	
Contribution to the Project	Trainer, physical therapist	
Funding Support	UMROI	
Kessler Foundation Research Center (KF)		**Status**
Name:	**Gail F. Forrest, PhD**	No change
Project Role:	Co-Investigator	
Nearest person month worked	1.2	
Contribution to the Project	Site PI	
Funding Support	KF	
Name:	**Leigh Ann Martinez**	No change
Project Role:	Site research coordinator	
Nearest person month worked	12	
Contribution to the Project	Recruitment, IRB administrative paperwork	
Funding Support	KF	
Name:	**Steven C. Kirshblum, MD**	No change
Project Role:	Site physician	
Nearest person month worked	0.36	
Contribution to the Project	Study physician/ medical examinations	
Funding Support	Kessler Institute for Rehabilitation	
Name:	**Jonathan Augustine**	No change
Project Role:	Research assistant	
Nearest person month worked	4	
Contribution to the Project	Primary trainer	
Funding Support	KF	
Name:	**Erica Garbrini, PT**	No change
Project Role:	Physical therapist	
Nearest person month worked	6	
Contribution to the Project	Primary trainer, physical therapist	
Funding Support	KF	
Name:	**Christopher Cirnigliaro, MS**	No change
Project Role:	Study assistant	
Nearest person month worked	2	
Contribution to the Project	Body composition assessments	
Funding Support	VA RR&D Center	

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period? Nothing to Report

What other organizations were involved as partners? Nothing to Report

Organization Name: Nothing to Report
Location of Organization: Nothing to Report
Partner's contribution to the project Nothing to Report
Financial support; Nothing to Report
In-kind support Nothing to Report
Facilities Nothing to Report
Collaboration Nothing to Report
Personnel exchanges Nothing to Report
Other Nothing to Report

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: N/A

QUAD CHART:

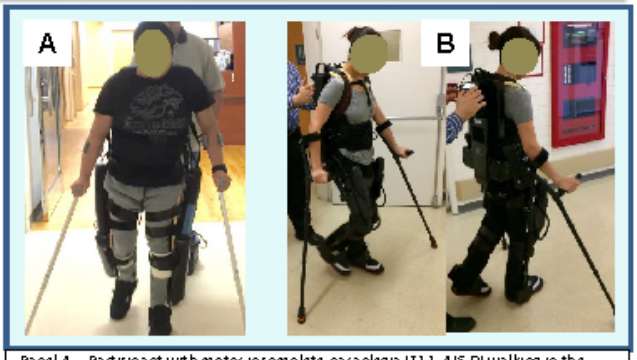
A Randomized, Crossover Clinical Trial of Exoskeletal-assisted Walking to Improve Mobility, Bowel Function and Cardio-Metabolic Profiles in Persons with SCI
Insert ERMS/Log Number and Task Title (Unknown)
SC130234
PI: Dr. Ann M. Spungen **Org:** Bronx Veterans Medical Research Foundation **Award Amount:** $1,555,889

Study/Product Aim(s)

The **primary objectives** are to achieve successful walking skills in the exoskeletal-assisted walking devices for an extended period of time and at specific velocities and distances over the course of 36 sessions in three months in people with chronic SCI who are wheelchair dependent for community mobility. The **secondary objectives** are to determine if this amount of walking is effective in improving bowel function and body composition.

Approach

A two-group, Phase III randomized clinical trial (RCT) is being performed using a crossover design with an exoskeletal-assisted walking intervention. Group 1 serves as the intervention follow-up to assess retention/non-retention of change due to the intervention on the outcome variables. Group 2 will serve as a lead-in to assess stability of the outcome variables prior to the intervention.



Panel A – Participant with motor incomplete paraplegia (T11, AIS D) walking in the ReWalk exoskeleton. Panel B- Participant with motor complete paraplegia (T3, AIS A) walking in the Ekso exoskeleton.

Timeline and Cost

Activities	FY 15	16	17	18
Text (12 participants enrolled)	Completed			
Text (30 participants to be enrolled)		Completed		
Text (48 participants to be enrolled)			45 of 48 Completed	
Text (64 participants to be enrolled)				
Estimated Budget ($K)	**$352**	**$371**	**$381**	**$263**

Updated: (September 30, 2017)

Goals/Milestones
FY16 Goals – Startup, kick-off and training meetings at each site; Initiate participant enrollment
☑ Q3-Participant screening and enrollment of 4 participants/site.
FY17 Goal – Continued participant screening and enrollment
☑ Q3-Participant screening, recruitment and enrollment of 8 (JJPVAMC), 4 (KF) and 6 (UMROI) participants per respective sites.
FY18 Goal – Continued enrollment
☑ Q1-Participant enrollment of 8 (JJPVAMC), 4 (KF) & 6 (UMROI)
☐ Q4-Participant enrollment of 8 (JJPVAMC), 4 (KF) & 4 (UMROI)
FY19 Goal – Completion of data collection
☐ Q2-Completion of participants
☐ Q3 to Q4 -Completion of data edits, analysis; Manuscript preparation
Comments/Challenges/Issues/Concerns - None
Budget Expenditure to Date
Projected Expenditure FY16 (Year 1): Approximate $352,335
Actual Expenditure FY16 (Year 1): Approximate $352,335

9. APPENDICES:

Appendix 1. Slide Presentation from ISCOS 2017

A Randomized, Crossover Clinical Trial of Exoskeletal-assisted Walking to Improve Mobility, Bowel Function and Cardio-Metabolic Profiles in Persons with SCI

Dr. Ann M. Spungen

VA Senior Research Scientist
James J Peters VA Medical Center, Bronx, NY

Vice Chair, Department of Rehabilitation Medicine
Icahn School of Medicine at Mount Sinai, New York, NY

Study Team - Acknowledgements

Site 1: Ann M. Spungen, EdD
James J. Peters VA Medical Center (JJPVAMC), Bronx, NY

Site 2: Peter Gorman, MD
University of Maryland Rehabilitation and Orthopaedic Institute (UMROI)

Site 3: Gail Forrest, PhD
Kessler Foundation (KF)

Co-Inv(s):
Jill M. Wecht, EdD (JJPVAMC)
William A. Bauman, MD (JJPVAMC)
Paula R. Geigle, PhD, PT (UMROI)

Study Objectives

Primary objective: Determine the walking/mobility skills at 12 and 36 sessions (not reported at ISCOS 2017)

Secondary objectives: Determine the effect on bowel function and body composition.

Exploratory objectives: Determine effects on vagal tone, bladder function, and lipid profile (HDL-c).

Outcome Assessments

- Bowel and Bladder Management (patient-reported outcomes using the SCI-QOL)
  - 5.0 (½ SD) reduction minimal clinically significant difference
  - 0.1 for any positive change
- Fat and Lean tissue mass (Dual energy x-ray absorptiometry, iDXA)
- HDL-c (Quest Diagnostic Laboratories)
  - 2.0 mg/dL minimal clinically significant difference

Results
Demographic Characteristics

Count	N=22
Age (y)	42 ± 15 (21 to 70)
Duration of Injury (y)	4.6 ± 4.3 (0.6 to 17.0)
Gender	5 Female, 17 Male
Level of Injury	
High Tetra (C5 and above)	5 (A, B, C, D)
Low Tetra (C6-C8)	2 (C, D)
High Para (T1-T6)	10 (A-D)
Low Para (T7 and below)	5 (A-D)
Total Steps in 36 sessions	47,943 ± 16,770 (22,633 to 78,630)

Results (n=22)
Bowel Management (SCI-QOL)

	N=22		
	n	%	Min Ch
Responders	6	27%	-5.0
NonResponders	16	73%	-5.0
Responders	14	64%	-2.5
NonResponders	8	36%	-2.5

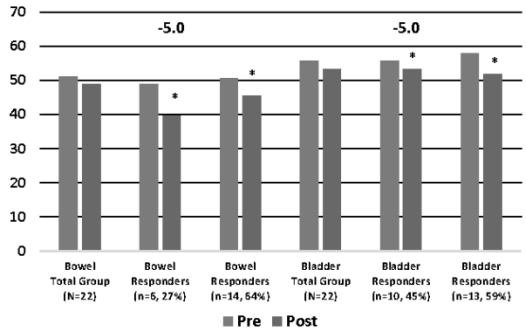
	Mean ± SD		
	Pre	Post	Change
Total Group (N=22)	51.0 ± 6.9	48.9 ± 8.7	-2.1 ± 5.2
Responders (n=6, 27%)	49.0 ± 5.6	39.7 ± 5.5	-9.3 ± 3.1
Responders (n=14, 64%)	50.7 ± 4.8	45.6 ± 6.8	-5.0 ± 3.9

Results (n=22)
Bladder Management (SCI-QOL)

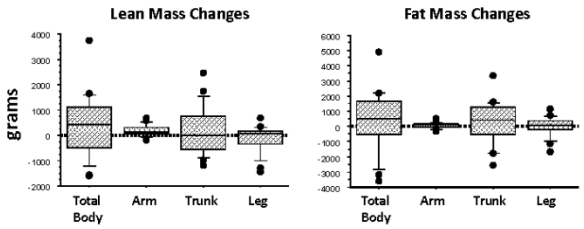
	N=22		
	n	%	Min Change
Responders	10	45%	-5.0
NonResponders	12	55%	-5.0
Responders	13	59%	-0.1
NonResponders	9	41%	-0.1

	Mean ± SD		
	Pre	Post	Change
Total Group (N=22)	55.7 ± 9.3	53.2 ± 8.6	-2.5 ± 5.9
Responders (n=10, 45%)	55.7 ± 9.3	53.2 ± 8.6	-7.5 ± 4.2
Responders (n=13, 59%)	57.9 ± 10.4	51.8 ± 8.8	-6.1 ± 4.2

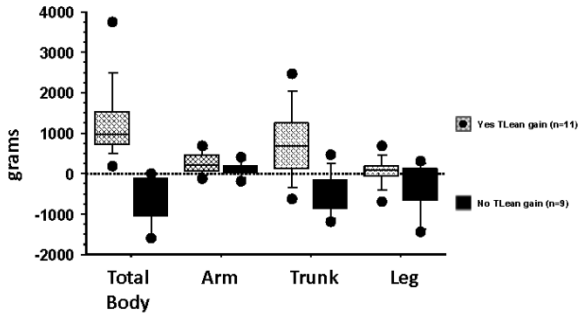
Bowel and Bladder SCI-QOL Changes



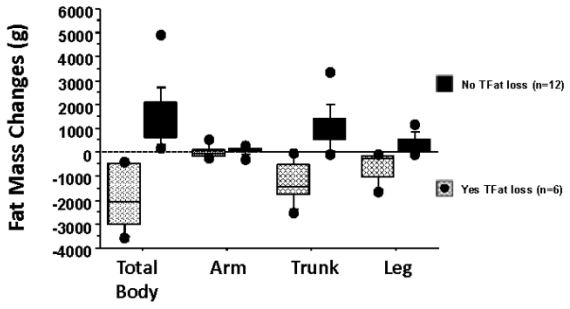
Results - Body Composition (n=20)



Lean Mass Changes Split by Responders



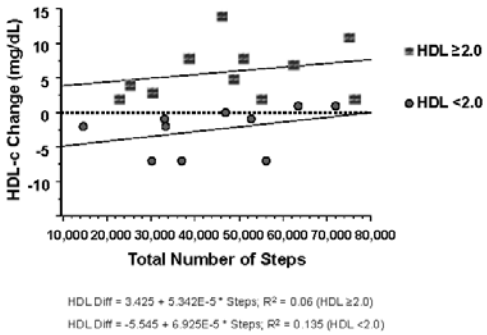
Fat Mass Changes Split by Responders



Results (n=21) - High Density Lipoprotein-cholesterol (HDL-c)

	PRE (mg/dL)	POST (mg/dL)
Mean ± SD	44.3 ± 10.7	46.1 ± 12.4
	Mean ± SD Diff	Range
Total Group (n=21)	1.9 ± 5.5	-7.0 to 14.0
Responders (n=11)	6.0 ± 4.0	2.0 to 14.0
NonResponders (n=10)	-2.5 ± 3.3	-7.0 to 1.0

HDL Split by Responders with Total Steps



HDL Diff = 3.425 + 5.342E-5 * Steps; R^2 = 0.06 (HDL ≥2.0)

HDL Diff = -5.545 + 6.925E-5 * Steps; R^2 = 0.135 (HDL <2.0)

Summary

- ✓**Bowel:** 27% had at least a 5 point and 64% reported a 2.5 point improvement
- ✓**Bladder:** 45% had at least a 5 point and 59% reported any improvement
- ✓**Lean:** 55% had an average lean gain of 1.2 kg
- ✓**Fat:** 30% had an average fat loss of 1.8 kg
- ✓**HDL-c:** 52% had an average HDL-c gain of 6.0 mg/dL

Conclusions

- **For those that are eligible, EAW provides a form of exercise that is well-tolerated and well-liked.**
- **Those that keep to the program have responses as expected with any exercise program.**
- **No effects for completeness or level of injury were found for bowel, bladder, lean, fat or HDL-c at this time.**

What we've learned so far…..

- Not everyone wishes to use one of these devices.
- Not everyone is eligible. There are clear contraindications for weight bearing activities in some individuals.
- Of those who are eligible and are taught to use these devices for walking, not everyone becomes proficient.
- With the same training protocol, some people have better responses than others.
- **For those who are eligible, have the time to participate or use one of these devices regularly, there appears to be important and significant medical, health and QOL benefits.**

Appendix 2. ASCIP 2017 Accepted Abstract Presentations

Patient-reported bladder management improvements after exoskeletal-assisted walking

EunKyoung Hong, PhD[1]; Steven Knezevic, MS[1]; Pierre Asselin, MS[1]; Christopher M. Cirnigliaro, MS, CEP, CBDT[1]; Stephen Kornfeld, DO[1,2,5]; Peter H. Gorman, MD[3]; Gail Forrest, PhD[4]; William A. Bauman, MD[1,5,6]; Ann M. Spungen, EdD[1,5]

[1]Spinal Cord Damage Research Center, James J. Peters VA Medical Center, Bronx, NY; [2]Spinal Cord Injury Service, James J. Peters VA Medical Center, Bronx, NY; [3]University of Maryland Rehabilitation Research Center, University of Maryland Rehabilitation and Orthopedic Institute, Baltimore, MD; [4]Kessler Foundation, West Orange, NJ; [5]Departments of Rehabilitation Medicine, Icahn School of Medicine at Mount Sinai, New York, NY; [6]Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, NY

Background: People with spinal cord injury (SCI) have difficulties with bladder management [1-3]. Depending on level and completeness of SCI, the bladder may be spastic, flaccid or a combination, resulting in time consuming care and unwanted voiding accidents or leakage between catheterizations. The SCI-QOL Physical-Medical Health Domain has a short form for Bladder Management Difficulties [4]. The influence of physical activity on bladder management and function in persons with SCI is largely unknown. The purpose of this study was to determine the effect of the three months of Exoskeletal Assisted Walking (EAW) on bladder management/function in people with chronic SCI.
Design: A two-group, crossover study design was employed. **Methods**: Fourteen participants with SCI were randomized to either EAW or usual activity (UA) first followed by crossover to the other intervention. Participants received 36 sessions of EAW over 12 weeks followed or proceeded by 12 weeks of UA. Patient-reported outcomes from the bladder SCI-QOL questionnaire (PRO bladder) were performed three times (baseline, at crossover, and after completion). A five-point decrease was considered to be clinically meaningful. The data was analyzed using Wilcoxon Signed Rank test and paired T-Tests. **Results:** The mean age of all participants was 42±16 years and the average duration of injury was 5±5 years. There were four with tetraplegia and ten with paraplegia. A greater proportion of participants reported a clinically meaningful change in bladder management (50% vs. 14%, p=0.059) across their EAW intervention compared with their UA. Across the EAW intervention arm, there was an overall average of 3.1±3.4 points improvement (55.5±7.2 vs. 52.3±7.3, p=0.008) in the PRO bladder. There were no clinical differences between the tetraplegic and paraplegic individuals' responses.
Conclusion: Thirty six sessions of EAW was associated with improved bladder management. These improvements included less interference with sleep, worry about an accident, limits to independence, and less time for bladder management functions. This preliminary work has implications for unexpected urologic quality of life improvements associated with EAW.

Support: Department of Defense/CDMRP SC130234 Award: W81XWH-14-2-0170 and National Center for the Medical Consequences of SCI (B9212-C, B2020-C), James J. Peters VA Medical Center

References:

1. Costa, P., et al., *Quality of life in spinal cord injury patients with urinary difficulties.* European Urology, 2000. **39**(1): p. 107-113.
2. Benevento, B.T. and M.L. Sipski, *Neurogenic bladder, neurogenic bowel, and sexual dysfunction in people with spinal cord injury.* Physical Therapy, 2002. **82**(6): p. 601.
3. Walter, J.S., et al., *A database of self-reported secondary medical problems among VA spinal cord injury patients: its role in clinical care and management.* JRRD, 2002. **39**(1): p. 53.
4. Tulsky, D.S., et al., *Development and psychometric characteristics of the SCI-QOL Bladder Management Difficulties and Bowel Management Difficulties item banks and short forms and the SCI-QOL Bladder Complications scale.* JSCM, 2015. **38**(3): p. 288-302.

Learning Objective: To determine the effect of EAW on bladder management.

Appendix 2. ASCIP 2017 Accepted Abstract Presentations

Increased serum high density lipoprotein after 36 exoskeletal-assisted walking sessions.

Steven Knezevic, MS[1]; Pierre Asselin, MS[1]; EunKyoung Hong, PhD[1]; Christopher M. Cirnigliaro, MS, CEP, CBDT[1]; Stephen Kornfeld, DO[2]; Peter H. Gorman, MD[3]; Gail Forrest, PhD[4]; William A. Bauman, MD[1,2,4,5]; Ann M. Spungen, EdD[1,5];

[1]Spinal Cord Damage Research Center, James J. Peters VA Medical Center, Bronx, NY; [2]Spinal Cord Injury Service, James J. Peters VA Medical Center, Bronx, NY; [3]University of Maryland School of Medicine, University of Maryland Rehabilitation and Orthopedic Institute, Baltimore, MD; [4]Kessler Foundation, West Orange, NJ; 5Departments of Medicine and Rehabilitation Medicine, Icahn School of Medicine at Mount Sinai, New York, NY

Background: Previous reports have shown that in persons with spinal cord injury (SCI), 64% with tetraplegia and 60% with paraplegia, had high density lipoprotein cholesterol (HDL-c) levels that were below 40 mg/dL; an independent risk factor for cardiovascular disease (CVD). As a result, persons with SCI have an increased risk for the development of CVD, which is one of the leading causes of death in the SCI population. Increased physical activity is an important factor associated with raising HDL-c levels. The effect of exoskeleton-assisted walking (EAW) on the lipid profile (LP) for serum total cholesterol (TC), triglycerides (TG), low density lipoprotein cholesterol (LDL-c) and HDL-c was examined.
Design: Prospective observational study in participants with chronic SCI.
Methods: Fifteen participants with SCI were recruited for study. Participants trained in the exoskeleton for 36 one-hour sessions in 12 weeks. Fasting blood samples were collected to determine serum HDL-c levels before and after completion of the 36-training sessions. Fasting serum samples were sent to Quest Diagnostics Laboratory for analysis using an automatic assay analyzer. For purpose of this work, a minimally clinically significant change was considered to be ≥2.0 mg/dL. Absolute values and a pre-post percent change were used to determine a clinically significant change.
Results: Greater than half (8 of 15) of the participants demonstrated a change ≥2.0 mg/dl in serum HDL-c levels. In the majority, HDL-c improved by an average of 6.5±4.4 mg/dL (ranging from 2.0 to 14.0 mg/dL). Although not statistically significant, those who had an improvement in serum HDL-c level walked for an average of 10,195 more steps than those who had no change (45,200±13,883 vs. 55,395±21,802, ns). No other significant changes were noted in the other lipid variables of TC, TG, and LDL-c.
Conclusion: The present study suggests that EAW of 3x a week for 12 weeks provides sufficient activity to favorably impact HDL-c levels in approximately half of those studied. Identifying successful methods to promote increased physical activity, improve serum HDL-c levels, and thus, reduce CVD risk would be anticipated to result in a healthier lifestyle and greater longevity in persons with SCI.

Support: DOD/CDMRP Award: W81XWH-14-2-0170/SC130234; VA RR&D National Center for the Medical Consequences of Spinal Cord Injury (B9212-C, B2020-C), James J. Peters VA Medical Center.
References:

- Bauman, W. A., et al. "Depressed serum high density lipoprotein cholesterol levels in veterans with spinal cord injury." *Spinal Cord* 30.10 (1992): 697-703.
- Bauman, W. A., and A. M. Spungen. "Coronary heart disease in individuals with spinal cord injury: assessment of risk factors." *Spinal Cord* 46.7 (2008): 466-476.
- Brenes, Gilbert, et al. "High density lipoprotein cholesterol concentrations in physically active and sedentary spinal cord injured patients." *Archives of physical medicine and rehabilitation* 67.7 (1986): 445-450.

Learning Objectives: Identify the practical applications of exoskeletons as therapeutic and clinical rehabilitation tools.

Appendix 2. ISCOS 2017 Accepted Abstract Presentations

ISCOS 2017 Workshop

A workshop duration is 90 minutes, with a maximum of **4 Speakers** (including chairperson and panelists).

Exoskeletal-Assisted Walking in Acute Inpatient and Chronic Outpatient Spinal Cord Injury Rehabilitation

Chester Ho, MD, Panelist (University of Calgary and Foothills Hospital, Alberta, Canada) will report on the safety and feasibility of exoskeletal-assisted walking (EAW) for gait training during acute, inpatient spinal cord injury (SCI) rehabilitation. A case series of six inpatients, who have participated in 25, one-hour EAW sessions using the Ekso, will be reported before and during EAW training for variables of blood pressure, skin integrity, exertion, and gait parameters. Preliminary results demonstrate that gait training with the exoskeleton is safe and feasible during the acute, inpatient phase after SCI.

Luciano Bissolotti, MD, Panelist (Casa di Cura Domus Salutis, Brescia, Italy) will report on the estimation of muscle fatigue in chronic, incomplete SCI by using sophisticated histogram analysis of quadriceps EMG signals of motor unit activation patterns before and after a single session of EAW training in the ReWalk exoskeleton. This work will shed light on the clinical significance of combined analysis of surface EMG and knee joint kinematics as a tool to understand muscle recruitment changes secondary to gait training with the ReWalk. Data may be useful for the prescription of a more precise rehabilitation gait training program in the clinical setting.

Gail F. Forrest, PhD, Panelist (UNDMJ-New Jersey Medical School and Kessler Foundation, West Orange, NJ) will report on 10 individuals with chronic, incomplete SCI who had a baseline lower extremity motor score of at least 1 and who have trained in either the Ekso or ReWalk for 100 hours. Gait data, kinematic and EMG changes for the lower and upper extremity after 50 hours and 100 hours of EAW training will be reported. In addition, data will also be presented for overground walking recovery on a subgroup of individuals.

Ann M. Spungen, EdD, Chairperson (JJP VA Medical Center, Bronx, NY and Icahn School of Medicine at Mount Sinai, NY) will report on 20 participants with chronic SCI who have completed 36, one-two hour sessions in three months of outpatient EAW training in either the Ekso or ReWalk for changes in the lipid profile, body composition by DXA, and patient reported outcomes of the SCI-QOL bowel and bladder surveys (DOD/CDMRP SC130234 Award: W81XWH-14-2-0170).